# Cystic Fibrosis and Newborn Screening

**What is CF?** Cystic Fibrosis is a treatable disorder that affects salt transport across cells lining secretory epithelial membranes. Abnormal secretions in pancreatic ducts, airways, intestines, and vas deferens lead to blocked lumens, organ injury, and dysfunction. CF is an autosomal recessive genetic condition caused by mutations in both copies of the CFTR gene. Both parents of a baby with CF are CFTR mutation carriers and other children may be affected.

**What is the incidence of CF?** CF occurs in 1/3,000 Caucasian, 1/6,000 Hispanic, 1/10,000 African-American, and 1/90,000 Asian-American births.

**What are the symptoms?** The most common presenting symptoms of CF are malabsorption diarrhea (due to pancreatic insufficiency) and failure to thrive, recurrent and chronic pulmonary problems, or a combination of both. The goal of newborn screening is detection and treatment of babies with CF *prior* to the onset of symptoms.

**What are Montana's CF statistics?** Montana has approximately 12,000 births per year and CF screening has been mandatory since January 2008. Five or fewer new cases of CF have been detected each year since 2008.

**What screening is performed at the Montana Public Health Laboratory?** CF screening in Montana uses a fluoroimmunoassay to measure the level of immunoreactive trysinogen (IRT) in dried blood spots. IRT is elevated in newborns with CF due to pancreatic dysfunction. An IRT level above a certain cutoff is analyzed in duplicate before an out of range result is reported and a second screen is requested. IRT levels decrease in the first weeks of life, but remain relatively high in babies with CF. If the IRT is elevated in both specimens, the baby's primary care provider is notified that further diagnostic testing for CF is indicated. *Most babies with abnormal IRT on the initial screen will not have CF*. IRT levels may be falsely elevated in premature or sick infants. Blood spots from infants with birth weights less than 1500 grams and two elevated IRTs will be automatically reflexed to CF DNA Mutation panel.

**How are IRT tests interpreted?** Normal ranges for IRT will change as of March 14, 2011 as a result of an expert statewide consultation. The MTPHL normal range for IRT on the first screen will remain less than or equal to 100 ng/mL, but the range will change to less than or equal to 80 ng/mL when the infant is greater than 7 days of age at collection. If the infant is greater than 21 days of age at collection, the normal range will be reduced to less than or equal to 70 ng/mL.

**What should happen if the first IRT screen is out-of-range?** A second specimen should be collected for screening by IRT. The recommended time frame for collecting the second screen has been shortened from 3 weeks to any time after 7 days, to reduce the delay between an out-of-range first screen and the repeat screen, which caused anxiety for families and providers. This also allows for an earlier referral for diagnostic CF testing if the second screen is out-of-range, and earlier treatment, if CF disease is confirmed.

**What tests are used to aid in a diagnosis of CF?** A sweat chloride test (the "gold standard" for CF diagnosis) is recommended for all Montana infants with persistently elevated IRT. Sweat is collected from infants by pilocarpine iontophoresis for quantitative chloride analysis. A chloride value greater than or equal to 60 meq/L makes the diagnosis, while a value of <30 meq/L effectively rules out CF. For a

minority of infants, chloride values will fall in an intermediate range (30–59 meq/L) and may prompt repeat testing.

DNA mutation analysis of the CFTR gene is another diagnostic method; however this may be problematic in patients with atypical mutations. Approximately 70 percent of CF is caused by a single mutation, ΔF508, but there are over 1,000 other mutations associated with CF. Detection of two deleterious mutations confirms the diagnosis, but detection of only one mutation may indicate a carrier state or an affected individual with an uncommon mutation on the second copy of the CF gene.

**Are there differences in the recommended screening protocol for low birth weight babies?** Diagnostic sweat testing is technically difficult for babies who weigh less than 2000 grams (approximately 5 lbs). If the initial and repeat IRT values are elevated in a baby with a birth weight of 1500 grams or less, reflex screening for CF DNA mutations will be done. An assay for 23 of the most common CF mutations will be performed on the second dried blood specimen. 98% of babies with CF should have at least one of these mutations. If two mutations are detected, CF is confirmed. If one mutation is detected, the baby is referred for further diagnostic evaluation. If no mutations are detected, CF is unlikely and no further testing is indicated.

**What treatment is available?** Treatment for CF depends on both the stage of the disease and the organs involved and can be coordinated by Montana's CF specialist and clinics along with the primary care provider. Infants with CF identified by newborn screening can receive pancreatic enzyme supplements, vitamins and a high calorie diet early in life so they can grow and stay healthy. They can also receive chest physiotherapy to clear mucous from the lungs as well as antibiotics to fight lung infection and drugs to thin the mucous and improve lung function.

**Will IRT screening alone find all cases of CF in newborns?** Montana's CF screening protocol is designed to detect as many newborns with CF as possible, but no screen is perfect. *Infants with symptoms suggesting CF (recurrent respiratory problems, failure to thrive, etc) should receive a CF workup and diagnostic testing, even if the newborn screen for CF was normal.*

**Whom should I contact if I have questions?** Please contact Linda Beischel, Newborn Screening Follow-up Coordinator at 800-821-7284 or 406-444-0984 with any questions or suggestions.